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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,348	01/19/2001	Dewen Qiu	19603/2986 (CRF D-1940B)	7683
7590 Michael L. Goldman NIXON PEABODY LLP Clinton Square P.O. Box 31051 Rochester, NY 14603			EXAMINER KUBELIK, ANNE R	
			ART UNIT	PAPER NUMBER
			1638	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/26/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/766,348

Applicant(s)

QIU ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41,49-51,53,58-61,69-71,73,75-77,80,82 and 84 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41,49-51,53,58-61,69-71,73,75-77,80,82 and 84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. In view of the new grounds of rejection presented in the Examiner's answer mailed 20 November 2006 and Applicant's reply under 37 CFR 1.111 filed on 22 January 2007, PROSECUTION IS HEREBY REOPENED.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 41, 49-51, 53, 58-61, 69-71, 73, 75-77, 80, 82 and 84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 November 2006, as applied to claims 41-47, 49-54, 58-73, 75-77 and 80-85. Applicant's arguments filed 22 January 2007 have been fully considered but they are not persuasive.

Neither the instant specification nor the originally filed claims appear to provide support for recitation of a "promoter that is not pathogen-inducible" in claims 41, 61 and 75, line 5. The only reference to plant promoters in the specification, on pg 36, line 19, states "various promoters including pathogen-induced promoters".

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Thus, at the time of filing, the only promoters contemplated were pathogen-induced promoters or promoters in general, which included pathogen-induced ones. Promoters other than pathogen-induced ones as a class were not part of the originally filed invention.

Thus, such a recitation constitutes new matter.

Applicant urges that various promoters, as recited in the specification, would include all types of promoters, including the constitutive promoters cited in the Exhibits to the Appeal Brief (response pg 6-7).

This is not found persuasive because the knowledge of those in skill in the art at the time of filing was that use of non-inducible promoters in expression of a harpin in a plant would kill the plant. The knowledge of the existence of constitutive promoters would suggest that Applicant would have mentioned constitutive promoters if they were contemplated at the time of filing.

Applicant urges that it was well known in the art that constitutive and other non-pathogen induced promoters were widely used for plant transformation, and thus various promoters” would be understood by those in the art to encompass non-pathogen inducible promoters; Koncz, Rogers and Fraley provide evidence that the instant application intended to cover use of both pathogen-inducible and nonpathogen inducible promoters (response pg 7).

This is not found persuasive because at the time of filing, one of ordinary skill in the art would have expected that use of constitutive promoters in expression of a harpin in a plant would kill the plant, as detailed in the 35 USC 112, 1st, enablement rejection. Thus, the instant specification would need to specifically mention constitutive promoters and/or other types of

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non-pathogen-inducible promoters for the instantly claimed invention to have been contemplated at the time of filing.

Applicant urges that no rule, guideline or case is cited to support the assertion that nonpathogen inducible promoters would need to be mentioned for nonpathogen inducible promoters to have been contemplated at the time of filing (response pg 8).

This is not found persuasive. The expectation that use of constitutive promoters in expression of a harpin in a plant would kill the plant, as detailed in the 35 USC 112, 1st, enablement rejection, is the reason for the need to mention nonpathogen inducible promoters

Applicant urges that at the time of filing it was conventional to use constitutive promoters and other nonpathogen inducible promoters in plant transformation; requiring recitation of the use of constitutive promoters appears to ignore the state of the art and the plain language of the specification (response pg 9).

This is not found persuasive because the state of the art was such that one of ordinary skill in the art would have expected that use of constitutive promoters in expression of a harpin in a plant would kill the plant, as detailed in the 35 USC 112, 1st, enablement rejection.

4. Claims 41, 49-51, 53, 58-61, 69-71, 73, 75-77, 80, 82 and 84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 November 2006, as applied to claims 41-47, 49-54, 58-73, 75-77 and 80-85.

Applicant's arguments filed 22 January 2007 have been fully considered but they are not persuasive.

The claims are broadly drawn to a method of imparting pathogen resistance to plants by planting a seed transformed with a construct comprising a nucleic acid encoding a hypersensitive response elicitor (harpin) of SEQ ID NO:1, 3, 5, or 7 and a non-pathogen inducible promoter and propagating a plant from the seed or by transformation of a plant with the construct.

The instant specification, however, only provides guidance for methods of treating seeds of a number of plant species with SEQ ID NO:1, growing the plant, exposing it to one of a variety of plant pathogens, and observing that plants grown from treated seeds with more pathogen resistant than plants grown from non-treated seeds (examples 1-8). The guidance related to expression of a nucleic acid encoding SEQ ID NO:1, 3, 5, or 7 in a plant is very general (specification, pg 36, line 6, to pg 37, line 12); however, plant transformation in general was well-known to those of skill in the art at the time of filing.

The instant specification fails to provide guidance for a method of imparting pathogen resistance to plants by planting a seed transformed with a construct comprising a nucleic acid encoding a hypersensitive response elicitor of SEQ ID NO:1, 3, 5, or 7 and a non-pathogen inducible promoter and propagating a plant from the seed or by transformation of a plant with the construct. Specifically, the specification fails to provide guidance for the use of a constitutive promoter in such constructs.

At the time of filing, constitutive expression of harpins in plants was considered lethal. For example, Bauer (US Patent 5, 850,015, filed June 1995) in discussing the expression in plants of a nucleic acid encoding the instant SEQ ID NO:1 states at column 13, lines 21-27:

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Transformation of plants with the DNA molecule of the present invention is particularly useful where the plant does not exhibit a hypersensitive response to pathogens or is weakly responsive to such pathogens. This requires that hrpN_{ech} be hooked up to the promotor of a plant gene that the pathogen induces such as PAL, CHS, etc. Otherwise, hrpN will kill the plant.

Beer et al (US Patent, 6,174,717, filed July 1992) expressed a similar belief that expression of HrpN would kill plant cells at column 24, lines 9-22):

Still another use would be the fusion of the gene encoding harpin to specific promoters of plant genes to develop specific transgenic plants. When the plant gene is "turned on", harpin would be expressed and the plant cell killed. Some appropriate plant gene promoters and their projected uses include genes involved in pollen development (resulting in the development of male sterile plants); genes that are expressed in response to infection by fungi, e.g. genes encoding phenylalanine ammonia lyase and chalcone synthase the plant cell would be killed thereby limiting the progress of the fungus and making the plant resistant to fungal diseases); and genes involved in the development of senescence (to facilitate harvest, expression of hrp genes would result in defoliation).

It is noted that two of the inventors on this patent are two of the instant inventors, Steven Beer and Zhong-Min Wei.

This view was prevalent until 2000, 3 years after the filing of the parent of the instant application. Tampakaki et al (2000, Molec. Plant Microbe Interact. 13:1366-1374) initially expressed a harpin in plants using an inducible promoter because they "expect[ed] that endogenously produced harpin may be lethal to the plant" (pg 1367, left column, paragraph 4), but to their amazement found that even when large amounts of the biologically active harpin was constitutively produced in plants, the plants showed no necrosis (pg 1367, left column, paragraph 4, to pg 1369, left column, paragraph 1).

Thus, given the state of the art at the time of filing, one of skill in the art would not have expected a constitutive promoter to function in the instant invention because one of skill in the

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art would have expected expression in a plant of a harpin from a constitutive promoter to kill the plant.

The instant specification makes no teaching as to the use of a constitutive promoter in expression of harpins in plants. Its only teaching with respect to plant promoters is the following on pg 36, lines 17-19:

As is conventional in the art, such transgenic plants would contain suitable vectors with various promoters including pathogen-induced promoters

Given the state of the art at the time of filing, use of non-inducible promoters would need to be taught by the specification.

The specification also does not teach any working examples in which a plant was transformed with a construct comprising a nucleic acid encoding a hypersensitive response elicitor (harpin) of SEQ ID NO:1, 3, 5, or 7 and a non-pathogen inducible promoter.

Given the state of the art at the time of filing, the amount of direction provided by the inventor in the specification, and the lack of existence of working examples, the instant invention is not enabled.

Applicant urges that Bauer and Beer do not represent the state of the art at the time of filing because they were filed in June 1995 and July 1992, respectively, both of which are substantially before the instant filing date of December 1997 (response pg 10).

This is not found persuasive. First, the instant application claims priority to 60/033230, which was filed 5 December 1996; thus, the effective filing date of the instant application is 5 December 1996, which is only 1.5 years after the filing date of Bauer. Second, Applicant did not submit any exhibits contradicting the position that at the time of filing, one of skill in the art would have expected expression in a plant of a harpin from a constitutive promoter to kill the

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plant. Additionally, Tampakaki et al's expectation that endogenously produced harpin would be lethal to the plant (pg 1367, left column, paragraph 4) shows that even several years later, one of skill in the art expected expression in a plant of a harpin from a constitutive promoter to kill the plant.

Applicant urges that at the time of filing the instant application, much more information was available regarding constitutive expression of HR elicitors in plants, citing the Declaration of Dr. Wei filed 16 August 2004, which states that the Nos promoter is considered a weak constitutive promoter and cites data showing that the expression of harpin from the nos promoter is not lethal (response pg 10).

This is not found persuasive because there is nothing in the Declaration showing that it was known at the time of filing that the expression of harpin from the nos promoter is not lethal.

Applicant urges that the statement in Tampakaki that it was expected that harpin may be lethal is not definitive, and Tampakaki does not state that it was the prevalent view that constitutive expression of harpin would be lethal or that only pathogen-induced promoters could be used - they was a chemical inducible promoter (response pg 10-11).

This is not found persuasive because Tampakaki's surprise in the lack of lethality is evidenced in their investigating whether the protein accumulated in plants in sufficient amounts (paragraph spanning pg 1367-1368 and paragraph spanning the columns on pg 1368) and their discovery that the expected necrosis only occurred when the harpin was produced in a excretable form (paragraph spanning pg 1369-1370). That researchers several years after the filing of the instant application assumed that constitutive expression of harpin in plants would be lethal is

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evidence that the state of the art at the time of filing was that of Bauer and Beer. Tampakaki's use of a chemically inducible promoter is further evidence that they expect

Applicant urges that the USPTO takes the view that an adequate teaching would require working examples, but this is not the case as expression of foreign genes in plants was well-known at the time of filing (response pg 11).

This is not found persuasive. A working example is another way in which Applicant could have demonstrated that constitutive promoters were enabled.

Conclusion

5. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
February 5, 2007



ANNE KUBELIK, PH.D.
PRIMARY EXAMINER